array location; and

ii) a population of microspheres comprising at least a first and a second subpopulation each comprising a bioactive agent;

wherein said microspheres are distributed on said surface such that said discrete sites each contain no more than one microsphere; and

c) determining the presence or absence of said target analyte.

REMARKS

Claims 18 through 34 are pending, and stand rejected. An appendix of the current claims has been attached for the Examiner's convenience. Favorable consideration of the following comments relative to the outstanding rejections as they may apply to the present claims is respectfully requested for the following reasons. A copy of the "Version to Show Changes Made" is also appended hereto as Appendix B for the Examiner's convenience.

Support for amended claims 18 and 19 can be found throughout the specification see for example in the "Summary of the Invention" on page 2, lines 34-36. Claims 18 and 19 were also amended for clarity, no new matter was added.

Rejection under 35 U.S.C. § 102(e) as anticipated by Walt et al.

Applicants respectfully traverse the rejection of claims 18, 20, 22, 23 and 28-32 under 35 U.S.C. § 102 as anticipated by Walt et al. U.S. Patent No. 6,023,540.

Examiner asserts that the Walt *et al.* patent discloses a "single, discrete, fiber optic bundle," and that such a bundle anticipates the presently claimed "substrate with a surface." Examiner further states that the Walt reference discloses that "microspheres may be optically coupled to discrete fibers or groups of fibers," and that groups of

fibers within a bundle anticipate the presently claimed "plurality of discrete sites."

Walt et al. discloses an optical fiber bundle sensor (element A or B) having wells (element C) etched in the end of the bundle into which microspheres can be distributed. Presence of an analyte can be determined by a change of the microsphere's optical signature in the presence of the analyte.

In contrast the present invention provides a plurality of assay locations (element A), each of which have a plurality of array locations (element B), each of which has a plurality of discrete sites (element C). In other words, the present invention discloses one more element than the Walt reference.

The law is well established that in order to anticipate a claim, the prior art must disclose "each and every element"of the claimed invention. SSIH Equipment S.A.v. U.S. Inc. Int'l. Trade Commission, 218 USPQ 678, 688 (Fed. Cir. 1983). As stated by the Federal Circuit in In re Bond, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990), "[f]or a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference." See also Glaverbel Societe Anonyme v. Northlake Marketing & Supply, Inc., 33 USPQ2d 1496 (Fed. Cir. 1995).

Here, "each and every element" is not present. The prior art reference is open to one of two interpretations (see attached sheet). In essence, the Examiner is combining both interpretations in order to say that the prior art reference has all three elements of the present invention. For example, the Examiner interprets "single, discrete, fiber optic bundle" (element B) of Walt, to be "substrate with a surface" (element A) of the present invention, and interprets "microspheres may be optically coupled to discrete fibers or groups of fibers"(element C) of Walt, to be "a plurality of assay locations" (element B) of the present invention. Examiner then revokes his initial comparison to interpret both "individual fibers"and "discrete fibers or groups of fibers," (element A) to be "a plurality of discrete sites" (element C). Examiner is inconsistant, because he takes one

element of the prior art and says it reads on two distinct elements of the present invention, by labeling one element of the prior art two different ways. That is, the Examiner interprets fibers or groups of fibers of Walt with both a substrate with a surface comprising a plurality of assay locations and a substrate with a surface comprising a plurality of discrete sites. This is an improper comparison. Either the "discrete fibers or groups of fibers" reads on "a plurality of array locations," in which case the element of a "plurality of discrete sites" is not present in Walt, or the "discrete fibers or groups of fibers"/"individual fibers" reads on "a substrate with a surface comprising discrete sites,"in which case the element of the "plurality of assay locations" is not present in Walt. Accordingly, the reference does not anticipate the present claims, and the rejection is improper. Applicants respectfully request the Examiner to withdraw the rejection.

Rejection under 35 U.S.C. § 103(a) as obvious over Walt et al., Geysen et al. and Brenner et al.

Claims 18-32 stand rejected under 35 U.S.C. § 103 as obvious over Walt et al. U.S. Patent No. 6,023,540, Geysen U.S. Patent No. 5,763,175, and Brenner U.S. Patent No. 5,763175.

Walt et al. is described above.

Geysen describes use of a library of hexapeptide sequences from a particular protein to detect antigen-antibody binding in a method for determining antigenically active peptides. Specifically, Geysen uses a 12 x 8 grid of peptide sequences attached to rods in such a way as to correspond to a microtiter plate. It is Applicants' understanding that the method of Geysen requires use of a single, different peptide sequence on each of the plurality of rods used in the method. Used in this manner, the one or more rods to which antibody binds will correspond to antigenically active peptides according to the respective sequence of the peptide attached to each rod.

Brenner describes a method for sequencing polynucleotides using oligonucleotide tags and tag complements on an array. The array contains spatially addressable locations on a solid support.

The Examiner suggests that it would have been obvious to use more than one fiber optic array and that the use of vessels to contain sample solutions would have been within the abilities of one of ordinary skill in the art as evidenced by Geysen. Applicants respectfully traverse.

The rejection under § 103 over the primary reference, Walt, assumes that the use of vessels to contain samples would have been within the abilities of one of ordinary skill in the art. Geysen and Brenner are provided as support for the Examiner's position. Applicants note that there are three requirements to establish a *prima facie* case of obviousness. These include that "there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." (MPEP § 2143). Applicants note that a rejection under § 103 based on a single prior art reference must be supported by some suggestion of the claimed invention or motivation to reach the claimed invention witch is found in that single prior art reference. *In re Laskowski*, 10 USPQ2d 1397 (CAFC 1989).

In this case Walt is silent with respect to any suggestion to increase or scale-up the number of analytes. Indeed, Walt demonstrates, as the Examiner noted, a sensor "that can support large numbers, thousands or more, of separate chemical functionalities." In addition, not all claim elements of the present invention are disclosed in the cited references. In Walt, either the "discrete fibers or groups of fibers" are analogous to "a plurality of array locations," in which case the element of a "plurality of discrete sites" is not present in Walt or the "discrete fibers or groups of

fibers"/"individual fibers" is analogous to "a substrate with a surface comprising discrete sites," in which case the element of the "Plurality of assay locations" is not present in Walt. *See* § 102 argument above. The Examiner is reminded that "the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. MPEP §2143.01.

Moreover, a statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art at the time the claimed invention was made because the references relied upon teach that all aspects of the claimed invention were individually known in the art" is not sufficient to establish a prima facie case of obviousness without some objective reason to combine the teachings of the *references. Ex parte Levengood,* 28 USPQ2d 1300 (Bd. Pat. App. &Inter. 1993). See also *In re Kotzab,* 217 F. 3d 1365, 1371, 55 USPQ2d 1313, 1318 (FED.Cir. 2000). The Examiner's broad assertion cannot be used to establish motivation to combine to come up with the specific assay set forth in the claims. Furthermore, the mere fact that Geysen, Brenner and Walt could be combined, does not render the combination obvious, because there is no suggestion in the prior art to combine the references.

In addition, Geysen and Brenner fail to teach a plurality of assay locations with array locations composing a plurality of discrete sites. Not all elements of the present invention are taught in the prior art references. Again, the Examiner interprets fibers or groups of fibers of Walt as both a substrate with a surface comprising a plurality of assay locations (element A) and a substrate with a surface comprising a plurality of discrete sites (element B). This is an improper comparison. Moreover, the prior art references do not provide motivation to modify Walt. Nowhere does Geysen or Brenner suggest the use of an array of arrays using a fiber optic bundle with discrete sites thereon.

Assuming *arguendo* that the cited references did suggest the combination

suggested by the Examiner to reach the instant invention, Applicant submits that the Examiner is attempting to create a hindsight reconstruction of the instant invention by piecing together references which in total may disclose all of the individual elements of the instant invention, yet in combination do not suggest that one of ordinary skill in the art would have a reasonable expectation of success. As stated in In re Fritch, 23 USPQ2d 1780 (Fed. Cir. 1992), "[I]t is impermissible to use the claimed invention as an instruction manual or `template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious." That is, at the time the application was filed there was no objective motivation found in the prior art to modify Walt to reach the claimed invention.

In view of the above, Applicants submit that the claims are not obvious over Walt et al. in view of the knowledge available to one skilled in the art as illustrated in Geysen. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejects Claims 20, 33, and 34 under 35 U.S.C. 112, first paragraph, arguing that the specification does not support the subject matter in the new claims. More specifically, that although page 13, lines 29-31 of the application disclose "a library of bioactive agents are used," that it does not disclose that each assay location comprises a library of bioactive agents. Applicants respectfully traverse the rejection.

The subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement. MPEP 2163.02. Rather, the test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisian that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ

177, 179 (Fed Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)).

The present invention provides a bead in each well (*e.g.* page 24, line 4); the beads have a bioactive agent (*e.g.* summary of the invention, page 2, lines 30-33 and page 4, lines 27-30); the bioactive agent can come from a library (*e.g.* page 12, lines 30-35). In a preferred embodiment a library is used (*e.g.* page 13, lines 13-16). Applicants submit that the specification would convey to one of skill in the art that applicants were in possession of the subject matter of claim 20, 33, and 34.

Rejection under 35 U.S.C. § 103(a) as unpatentable over Walt et al.

Claims 33 and 34 stand rejected under 35 U.S.C. 103(a) as unpatentable over Walt *et al.*. More specifically, Examiner argues that the reference teaches a microsphere-based analytical chemistry system including an optical encoding and an optical fiber bundle sensor, and that one skilled in the art would have been motivated to assay a library of bioactive active agents at each assay location, because the specifications states "in the presence of one or more" substrates at column 14, lines 16-17, and that the sensors may be used diagnostically in column 9, line 60 through column 10, line 3. Applicants respectfully traverse.

Walt *et al.* has been discussed in detail above.

The elements of a 103 rejection were set forth above. Again, the three requirements to establish a *prima facie* case of obviousness are: "suggestion or motivation," "a reasonable expectation of success," and " teach or suggest all the claim limitations." (MPEP § 2143).

Claims 33 and 34 depend from the claims that were argued above. Again, there was not As described previously, Walt does not render the present claims obvious

because no motivation exists, nor are all elements of the present invention cited in Walt.

CONCLUSION

Applicants submit that the claims are now in condition for allowance and an early notification of such is solicited. Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,

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